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SOME PITFALLS IN THE DIAGNOSIS AND TREATMENT OF INHERITED SYPHILIS

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MR. PRESIDENT, LADIES AND GENTLEMEN,

I hope you will not be disappointed when you will have heard my address this evening, that I have nothing novel or startling to tell you with regard to the symptomatology, diagnosis or treatment of inherited syphilis, but having closely studied over 1,000 cases of the disease during the years that I have been in charge of the V.D. Clinic at the Hospital for Sick Children, Great Ormond Street, it occurred to me that I might usefully bring to your notice some of the lessons which I have learnt from this considerable volume of clinical material. At the present day when we possess the great advantages over our predecessors in having as aids to diagnosis the possibility of demonstrating the *Treponema pallidum* in certain of the lesions, the Wassermann and other blood tests, as well as the clinical experience which the application of these pathological investigations has enabled us to accumulate during the past twenty years, the diagnosis of inherited syphilis is often a very simple matter. In some cases, on the other hand, it is not easy, or perhaps one should say, it is not obvious, and the disease is consequently overlooked, yet if it is borne in mind and the case appropriately investigated the diagnosis is easily made. When we bear in mind the enormous advantage which the present generation of practitioners possesses over those of bygone days, and find that even now cases are frequently missed, we cannot but admire the great ability and clinical acumen of such men as Ricord, Colles, Fournier, and Jonathan Hutchinson, to mention only some of them, who did so much to advance our knowledge of inherited syphilis.

It may be of interest to enquire into the stages whereby

BRITISH JOURNAL OF VENEREAL DISEASES

the present state of our knowledge of inherited syphilis has been reached, for by so doing we shall be able to appreciate some of the pitfalls which beset the physicians of previous generations. Soon after the alleged importation of syphilis into Europe from the West Indies by the sailors of Columbus, the occurrence of syphilis in new-born children was recognised. Diday in his Treatise on Syphilis in new-born Children states that Torella (1498) was the first to mention the existence of syphilis in new-born infants, but like other writers of that period he believed the disease was transmitted by an infected nurse through a local sore. Other writers of that period held that the infection occurred solely through the nurse's milk.

Paracelsus (1529) was the first to assert positively the hereditary nature of the disease, but it was many years before this view became generally recognised. Practically all the writers upon the subject of the sixteenth and seventeenth centuries concerned themselves mainly with the mode of transmission of the disease to children: whether by the nurse—and if so, through the milk, or by direct contact; or *per generationem*, directly from the father or from the latter *via* the mother; or whether from father and mother; they didn't trouble much about symptoms. Rosen von Rosenstein,* was the first to refer more particularly to the symptoms of inherited syphilis, with a good description of the infantile skin lesions, and in addition he refers to a case of late inherited syphilis in a girl of eleven who had caries of the palate and nasal bones, ulceration of the face and enlarged glands in the neck. Mercury is being used in treatment, and he also recommends mercury rubbings for the mother during pregnancy to safeguard the child.

Rosen observed that, and endeavours to explain why, in a family some of the children are healthy and others syphilitic, and he appears to have realised the possible influence of syphilis upon the nervous system or upon the mind. I should like to quote his own words. "In one case the contagion in the parents is very much weakened, though not quite extinct, by means of a very good diet and of some remedies; therefore it may at another time be again kindled by an irregular diet or some other means

* Rosen von Rosenstein. "The Diseases of Children and their Remedies." The Swedish edition of 1771 translated by Andrew Sparrman, 1776.

TREATMENT OF INHERITED SYPHILIS

. . . . that a child born at such a time will be brought into the world dead or with the above mentioned foul disorder. This is the reason that of several children of the same parents which are in this unhappy condition, some enjoy a perfect health, whilst both the body and senses of the other are affected." One cannot say exactly what he means by senses ; it may mean the sense organs and refer to ophthalmia, but I think not, for that would be included under affections of the body. It would appear justifiable to conclude that "senses" refers to mind as opposed to body and that Rosen was familiar with the influence of inherited syphilis in the causation of mental defects.

An impetus to the study of venereal diseases in mothers and infants was given by the establishment by Lenoir of a special hospital at Vaugirard, in Paris, for the reception and treatment of expectant mothers and their offspring. This was about the year 1780, and according to Bertin, who was one of the physicians to the institution, and who has given us a glowing account of the good work carried out in that hospital in a book published in 1810, the three doctors who had charge of the patients before Bertin himself arrived on the scene, namely Colombier, Doublet and Faguer, all recognised ophthalmia as one of the most frequent symptoms of venereal disease in infants. It would appear therefore that just as in adults, syphilis and gonorrhœa were thought to be due to one and the same virus, so in the newly born, the symptoms of venereal disease were *all* thought to be due to one cause, viz., syphilis. This, which we now know to be incorrect, is an excusable error, which was taught well into the nineteenth century.

Bertin appears to have been a keen and accurate observer, for he gives a detailed description of the symptoms of inherited syphilis as recognised by him, and he includes the various lesions of the skin and nails, mucous membranes of the eyes, nose and genital regions (urethra and anus), buboes and the bones. He lays particular stress on ophthalmia, which he says is often serious and may lead to blindness. He certainly saw and recognised syphilitic osteoperiostitis and records a case in a child five weeks old, with ophthalmia, pustules all over the body, a tumour over the left great trochanter and a periostitis on the front and back of the elbow. The

BRITISH JOURNAL OF VENEREAL DISEASES

swelling of the trochanter disappeared in about a month, but the lesion of the elbow was more resistant to treatment. This consisted in mercury rubbings applied to the nurse, which mode of treatment, according to Bertin, was first suggested by Garnier. As the elbow and skin lesions both persisted for another month the infant was given Van Swieten's mixture for three months, when all the symptoms disappeared.

It is a curious fact, however, that other writers of this period and even considerably later (*vide* Diday, 1858; Robert, 1861), do not lay much stress on epiphysitis in syphilitic infants. Diday and Robert both quote Bertin's case mentioned above, and the latter remarks that others have cited similar cases, but such cases appear to have been regarded as rarities. Nowadays a large proportion of syphilitic infants are known to suffer from osteoperiostitis or epiphysitis (Cooke and Jeans, 20 per cent. of infants under two) and as it is unlikely that so obvious a manifestation as psuedo-paralysis or epiphysitis would have been overlooked by all the older syphilologists, it may be justifiable to conclude that epiphysitis did not so commonly occur in congenital syphilis at that time. Perhaps it was partly due to the fact that so many of the children died at a very early age from the severity of the disease, and partly to the fact that the bone lesions which did occur were ascribed to rickets (Parrot).

Bertin is of the opinion that the locus of the symptoms varies with the mode of infection, thus, if this is intra-uterine, there will be the manifestations of general syphilisation, skin lesions, coryza, sallow complexion, cachexia; if, on the other hand, the babe is affected during parturition when passing through the maternal passages, there will be blenorrrhagias of the eyes or of the genital organs and buboes; and thirdly, if infection comes later through a nurse, the initial lesion may be in or near the mouth or on some other part of the body, if produced by contact with a sore on the nurse. He does not believe much in the "old man" look, which Doublet aptly described as "*La miniature de la décrepitude.*" Bertin maintains you may get it in other conditions, especially shortly before death.

He recognises that there may be an incubation period of several weeks after birth before syphilitic symptoms appear, the mother never showing any signs of venereal

TREATMENT OF INHERITED SYPHILIS

disease, but the father having had constitutional symptoms of syphilis. He adds, "I regard this as one of the best established observations in medicine."

With regard to ophthalmia neonatorum, I have already mentioned that Bertin regards this as one of the commonest symptoms observed in children born of syphilitic parents, but he noted that mercury appears to have no beneficial influence upon it, yet it is advisable to give mercury in these cases to prevent possible sequelæ. These of course would be of a syphilitic nature, and these remarks of Bertin show that in those days, as I believe is often the case to-day, parents had a mixed infection of syphilis and gonorrhœa and that in consequence the children of such doubly infected mothers could show signs of both forms of venereal disease. I have had a few cases of children with inherited syphilis who have been blind almost from birth as a result of ophthalmia neonatorum. In spite of his observation that mercury did not benefit ophthalmia, yet did cure cases with constitutional, *i.e.*, syphilitic, manifestations, he considers that the identity of the viruses cannot be doubted, for he instances the case of a woman who, apparently suffering only from gonorrhœa, was able to infect two men with whom she had sexual relations within a short interval of time, the one with gonorrhœa and the other with a chancre. He then goes on to say that Hunter claims to have produced chancres by inoculating the pus of a recent gonorrhœa, but he, Bertin, does not agree, as he tried this experiment several times without success.

I have given this rather detailed extract from Bertin's work because it shows what was the prevalent teaching about the year 1810. About fifty years later we find two other important works on syphilis, *viz.*, that by Diday, of which an English translation by Whitley was published in 1859, entitled, "A Treatise on Syphilis in New-born Children," and the other by M. Robert, published in 1861, based on the records of cases occurring in Ricord's clinic.

Diday gives a very good description of the symptoms of early inherited syphilis, but adds that "syphilitic lesions of the bones, so common in adults, are extremely rare in infants. One scarcely finds them mentioned at all in any special book on this subject, and the annals of

BRITISH JOURNAL OF VENEREAL DISEASES

science offer, at most, five or six well authenticated instances."

Among the visceral lesions he states that Lagneau, Jun. and Depaul in 1851 described various forms of pulmonary affection; Dubois (1850) suppuration of the thymus; Gubler (1848) described the syphilitic liver, which Trousseau, Heurteloup and others also described, and that Simpson, in the *Edinburgh Medical and Surgical Journal*, No. 137, described several cases of peritonitis. In the chapter on retarded or latent congenital syphilis, he says that the first three months is the usual age, and six months is the latest age at which a congenitally syphilitic child may show constitutional symptoms, but he adds that some authorities admit a form of congenital syphilis arising even in adult life. Others say that congenital syphilis may, by combining with certain diatheses, give rise to scrofula, peculiar debility, etc.

He gives examples of alleged delayed congenital syphilis from various earlier and contemporary writers, but he evidently does not believe much, if at all, in this delayed form of the disease for he says, "cases of this kind are all more or less subject to doubt. This is no reason, however, for failing to take note of them." Amongst the various cases he cites from other writers, is one reported by Trousseau, in 1826, of a girl of nineteen with a "chancre" in the throat. At the age of six years she had exostoses on the legs. Trousseau says she probably had hereditary syphilis or syphilis acquired at the time of her birth. This is the earliest record I have been able to discover of the periostitis we now associate with congenital syphilis in older children. Various authors quote instances of ulceration of the pharynx and palate (Rosen von Rosenstein, it will be remembered, recorded such a case already, in 1771), and the so-called "chancre" in the throat in Trousseau's patient of nineteen may possibly have been an instance of ulceration of the pharynx.

Diday adds that a host of lesions in children have been ascribed to the results of syphilis in the parents: Doublet, induration of the cellular tissue; Astruc, rickets and tabes; Pitschaft, obstinate insomnia; Campbell, convulsions; Haase, hemicrania and hydrocephalus; and lastly Sanchez, who ascribes imperforate anus, hypospadias, and even the green stools of new-born children to the venereal virus!

TREATMENT OF INHERITED SYPHILIS

From Robert's "*Nouveau Traité*," published in 1861, we learn that Ricord commenced his investigations on the inoculability of venereal matter in 1832, and as a result of these investigations he disproved Hunter's thesis that gonorrhœa and syphilis were one and the same disease. During the earlier period of his work Ricord held the view that of all the lesions, the primary lesion is alone inoculable, but in 1859 a Committee of enquiry, of which Ricord was a member, reported to the French Imperial Academy of Medicine that the secondary or constitutional lesions of syphilis are manifestly contagious and that the mucous tubercle or condyloma is the most contagious of them all. Robert adds very little to the then existing knowledge of the symptoms of congenital syphilis, and although Jonathan Hutchinson had already begun to write articles from 1852 onwards on the lesions of the eyes and teeth in the subjects of inherited syphilis, these had not yet gathered sufficient momentum to cross the Channel and impress the continental syphilologists. Robert makes practically no mention of the late manifestations of inherited syphilis, but gives two cases, one a lady of sixty-five with a painful swelling of the knee which yielded only to treatment with potassium iodide, and the other a lady of forty-two with a perforation of the palate which cleared up on the administration of the same drug, both of which he regards as instances of delayed congenital syphilis, for he naïvely asks "if it is unreasonable to ascribe those two cases to hereditary syphilis as there is no history of acquired syphilis in the patients or their husbands!"

Undoubtedly the two greatest names in connection with our subject are Jonathan Hutchinson and Alfred Fournier, the two pillars of the syphilitic edifice of pre-spirochæte and pre-Wassermann days. Hutchinson, as is well known, was the first to draw attention to the fact that interstitial keratitis—which until his time was known as strumous corneitis—was nearly always due to inherited syphilis. He was the first, too, to describe the peculiar type of teeth we now associate with his name, and he states that interstitial keratitis is almost invariably coincident with the syphilitic type of teeth and that deafness is also a common accompaniment of these two manifestations, the three being known as the Hutchinsonian triad. He also foreshadows the possible effects of syphilis

BRITISH JOURNAL OF VENEREAL DISEASES

upon the endocrine glands in his aphorism 37, which says, "It is probable that the arrest of growth, when it does occur, is not due immediately to contaminated blood, but to the indirect influence upon nutrition of impaired organs (more especially the skin and the liver) which have been damaged by syphilitic inflammation." He also drew attention to the occurrence of acute iritis and of hydrocephalus in congenitally syphilitic infants. His book, "A Clinical Memoir on Certain Diseases of the Eye and Ear, consequent upon Inherited Syphilis," was published in 1863, though he tells us that he commenced to write papers on these subjects in the year 1852. Fournier started under Ricord, and like Hutchinson, maintained his interest in syphilis throughout life. He drew particular attention to, and in 1886 wrote a treatise upon, the symptoms of late congenital syphilis. It is a curious fact that as late as 1886, that is, twenty-three years after the publication of Hutchinson's book, the Hutchinsonian teeth were hardly recognised in France except by a few syphilologists and dentists. Fournier refers to them in his book, but adds that Parrot had described similar teeth among the deciduous set, and that he himself agrees with that observation.

Although Fournier mentions cases of hydrarthrosis affecting the knees more particularly, it was Clutton who, in a paper written in 1886, drew special attention to the occurrence of this manifestation of late inherited syphilis.

In 1872, Parrot published in the *Archives de Physiologie*, his memoir on "Pseudo-paralysis caused by an alteration of the Bones in Congenitally Syphilitic Infants." At first he was of the opinion that *every* case of inherited syphilis had these bone lesions, but he subsequently modified this opinion slightly and substituted the words "most cases" for "every case."

In May, 1879, Parrot read a paper before the Pathological Society of London on the bony lesions in hereditary syphilis. In that paper he mentions that prior to 1870 isolated cases of bony changes in the long bones in syphilis had been recorded by various observers, but that Wegner was the first to publish in Virchow's Archives for 1870 an account of the pathology of the condition.

Dr. (now Sir Thomas) Barlow and Dr. Lees, at the same meeting of the Pathological Society (May, 1879), read a paper on lesions of the cranial bones in congenital

TREATMENT OF INHERITED SYPHILIS

syphilis, and at a previous meeting of the same society (in March, 1879) Dr. Barlow showed specimens of disease of the skull in congenital syphilis. He described the Parrot's nodes which are due to osteophytic growths at the boundaries of the anterior fontanelle on the frontal and parietal bones, extending backwards to a variable extent parallel to the sagittal suture. These give rise to the natiform or hot-cross-bun head. It is interesting to record that the Museum of the Hospital for Sick Children, Great Ormond Street, possesses a case containing a number of Parrot's original specimens of foetal and infantile syphilitic bones, which that distinguished French physician presented to the Hospital.

Lastly, we may mention that Fournier was well acquainted with the effect of inherited syphilis on the brain and spinal cord, but he is rather apt to ascribe all or most nervous and mental symptoms in children to syphilis or parasyphilis.

Coming now to the practical part of my subject: to which cause or causes may the difficulties or errors in the diagnosis of inherited syphilis be due? Undoubtedly there are several factors, one or more of which may be operative in any specific instance. The errors may be those of omission or of commission; the former, that is to say, the failure to diagnose inherited syphilis when present, being in my experience far more common than the latter. The sources of error may be due to various causes, first the inherent difficulty of the case, the symptoms being either unusual or very mild; secondly, want of experience, knowledge or appreciation of certain symptoms and signs; thirdly, the exercise of insufficient care in the examination of the patient; and fourthly, the omission to think of the possibility of inherited syphilis. To take the last cause first, this may be partly due to the fact that cases of syphilis, once they are diagnosed in the out-patients' departments, are transferred to the special V.D. clinics, where they are more or less lost as teaching material. The result is that unless a student attends the V.D. clinic regularly he fails to follow the progress of the cases, which in consequence are not impressed on his memory as they should be.

The first two causes will be considered more in detail later on when describing cases which have actually come under the writer's notice. The third cause, namely, the

BRITISH JOURNAL OF VENEREAL DISEASES

exercise of insufficient care in the examination of the patient implies the omission of the physician or surgeon to invoke the aid of the pathologist and radiologist to assist in making the diagnosis by means of an investigation of the blood or spinal fluid in the one case, and of the bones in the other case. Why is this? Some clinicians undoubtedly have the clinical instinct extraordinarily well developed and can diagnose the disease at a glance, yet at times that clinical instinct may play them false and make their diagnosis incorrect. A blood test of the child and mother might have prevented such a mistake in diagnosis. In any event, if the case be undoubtedly clinically syphilis, the positive blood test would be a confirmatory symptom and, moreover, would be useful, nay essential, as the beginning of a series of tests which should be employed during the progress of the treatment to determine when that treatment could be safely stopped.

Clinicians have occasionally told me that they do not believe in the Wassermann test, because they have received conflicting reports from different pathologists upon the same sample of blood. This may well be and only serves to emphasise the fact that these serological tests, which are undoubtedly complicated, should be entrusted to, and be carried out by, reliable pathologists only. Possibly the pædiatricians who express disbelief in the serological tests are to some extent actuated by their dislike of having their little patients pricked, but when skilfully performed, the operation of blood-taking gives rise to only a minimum of pain and discomfort to the child, whereas the benefit to the patient of making a correct diagnosis and of giving appropriate treatment at the earliest possible moment, may be of the greatest value to his future health and well-being. Conversely, failure to diagnose inherited syphilis in infancy may lead to early death or, what is perhaps worse, to a life of chronic suffering and invalidism. W. P. Lucas, in an unpublished study of Juvenile Syphilis, referred to by the Solomons in their book, "Syphilis of the Innocent," 1922, investigated 885 cases of the disease during the decade 1902-11, that is, in the pre-Wassermann and early Wassermann days. Fifty per cent. of these cases occurred in children one year old or under, the remaining 50 per cent. were scattered through the later years, and one can

TREATMENT OF INHERITED SYPHILIS

safely say that if routine Wassermann had been carried out on these children, the majority, if not all, of these cases could have been diagnosed in infancy.

A fruitful source of error in diagnosis is the still prevalent doctrine that the obstetric history of a syphilitic mother follows what is sometimes known as Kassowitz' law. According to this law, which was formulated by Kassowitz in 1876, but which had already been outlined by Jonathan Hutchinson in 1863, the virus of syphilis becomes progressively attenuated the more distant is the date of infection in the parent, with the result that the effects upon the children are progressively less harmful. The usual teaching is that a period of sterility may follow the infection, then a series of early abortions, later on miscarriages at four to seven months, then a still-born child at term, and after this a living syphilitic child. This sequence of events may rarely occur, but it is by no means the rule, though undoubtedly one or two abortions or miscarriages may precede the birth of a living syphilitic child. The writer has, however, seen very many instances in which the syphilitic child brought to hospital has been the result of the first pregnancy, and he has also seen cases of severe and even fatal syphilis in infants born to an apparently healthy mother, after the birth of one or more children, who are subsequently discovered to have latent syphilis with a positive W.R.

While admitting that the severer infections are more likely to occur first, and the milder ones later, I think Kassowitz' law should not be too strongly emphasised, but that the teaching should be: first, that one or more abortions or miscarriages before the patient should make one suspect syphilis and therefore examine the patient thoroughly from that point of view; and secondly, the fact that the patient is the first child, and there is no history of previous miscarriages, by no means denies the possibility of syphilis. I have gone into this matter rather fully because I have seen the mistake made so often, even in hospital practice.

Let us consider now some of the individual symptoms of inherited syphilis and how mistakes in diagnosis may be made. A child may be born with a rash—erythematous, papular or bullous-snuffles and marasmus. Such cases are usually easily diagnosed and are often rapidly fatal. When, as is much more frequently the case, the

BRITISH JOURNAL OF VENEREAL DISEASES

child is born apparently healthy and develops snuffles and a rash some weeks later, the latter may have to be diagnosed from the so-called "napkin-rash," which is usually of a brighter hue than the syphilitic rash, and does not spread so far on the thighs, legs and abdomen. The crusted nose, hoarse or aphonic cry and the cachexia are all in favour of syphilis. The napkin rash, ammoniacal dermatitis or Jacquet's erythema, to give it the different names by which it is called, may assume various forms; erythematous, erythematovesicular, papular or ulcerative. According to Jacquet, Trousseau described the papular form and Parrot the ulcerative, and both were mistaken for syphilitic lesions. This dermatitis affects mainly the convex areas, and is almost certainly due to irritation by the urine. We had such a case recently in the wards at Great Ormond Street in a child three months old; the lesions were papular and were diagnosed by the physician in charge as condylomata, even though the W.R. in mother and child were negative. Condylomata are not very commonly met with in children and in our experience at Great Ormond Street are rarely seen before the age of one year. The appearance of the lesion is usually quite characteristic and the failure to diagnose it can only be attributed to gross ignorance or carelessness. Quite a number of cases have been brought to hospital because the child was thought to be suffering from "piles."

Last year we saw two cases of condylomata within the space of a month. The first was a little girl aged one year and seven months who had had a condyloma for five months. She had been seen by several doctors, including some at an infirmary, and had been unsuccessfully treated with zinc and other ointments. The second case was also a girl, aged one year and nine months, whose condyloma was missed by a private practitioner and later by a large general hospital. This patient was found to have a positive W.R. in the cerebro-spinal fluid as well as in the blood. Both cases cleared rapidly with arsenic injections and pills of mercury iodide.

Coming now to the bone lesions in early inherited syphilis, it has been mentioned above that already in 1810, Bertin described a case of osteoperiostitis of the femur and elbow in a child aged five weeks, yet in 1860, writers such as Diday and Robert almost doubt, or

TREATMENT OF INHERITED SYPHILIS

grudgingly admit, the possible occurrence of this lesion. Nowadays we regard this as a common symptom of the disease and some authorities even hold that it is present in every case. Certainly, if systematic X-ray examinations be made of all cases of inherited syphilis under the age of six months a very considerable proportion of the infants will show unmistakable evidence of syphilitic osteoperiostitis or epiphysitis. On several occasions I have thus discovered X-ray evidence of periostitis in the absence of pain or tenderness of the limbs, or of any clinical manifestation of epiphysitis.

Two interesting and instructive cases of this lesion may be cited. A child was born to a known syphilitic mother on December 16th, 1927. On January 24th, 1928, the infant appeared healthy and the W.R. was negative. On March 26th, that is at the age of three and a half months, the right leg was painful and tender, on account of which the mother brought the child again to the clinic. There was now some snuffling, but no rash; X-rays showed periostitis of the right tibia: the blood W.R. was now very strongly positive (4.4.4.4), the cerebro-spinal fluid negative. Antisyphilitic treatment was immediately started with the result that in a week the leg was no longer tender and the snuffles ceased. The subperiosteal exudate increased, however, and on April 4th was more extensive than on March 27th. By the end of June the periostitis had not yet entirely subsided, but the child apparently suffered no inconvenience after the first week of its onset. All subsequent blood tests, two in 1928, three in 1929 and one in 1930 have been negative, and it is instructive to note that the only positive W.R. recorded coincided with the onset of the periostitis.

The other interesting case of epiphysitis was that of a child born in a maternity hospital (January 30th, 1929), healthy at birth and for two months afterwards. Then it did not move its left leg, or as the mother described it, "held it stiff," and the child cried when touched. There were no snuffles or rash. The patient was admitted to a surgical ward on account of "inability to use the left leg and with marked muscular spasm," the clinical diagnosis being "injury to the left hip joint or upper end of femur." An X-ray investigation cleared up the obscurity of the case, for it demonstrated the presence of

BRITISH JOURNAL OF VENEREAL DISEASES

osteitis and periostitis of the long bones of the lower limbs—suggesting syphilis. The presence of anæmia with enlargement of the liver and spleen suggested to some of those who saw the patient a condition of von Jaksch's anæmia, but all the symptoms were undoubtedly due to syphilis, for the bones have cleared up, the liver and spleen are much smaller and on 18.3.30 the W.R. was negative, and the child's condition was quite satisfactory except for delayed dentition.

Another symptom which may be associated with inherited syphilis in early childhood is a mild hydrocephalus, and although this is mentioned in most of the recent books and articles on congenital syphilis, it does not appear to be generally appreciated that this condition may be due in quite a considerable proportion of cases to this disease. Jonathan Hutchinson wrote in 1863, "Chronic arachnitis as evinced by a tendency to hydrocephalus is very common in syphilitic infants and occurs in almost all who suffer severely from the taint in question." I have come across quite a number of instances where a Wassermann was not asked for until several months after the child had first attended the out-patients' department of a hospital, and when investigated it has been found positive in the blood and generally also in the cerebro-spinal fluid.

This brings one to the question of cerebro-spinal syphilis in the inherited form of the disease, which is not only much more prevalent than is generally realised, but unfortunately is the aspect of inherited syphilis which gives rise to the most tragic consequences in children. A neglected cerebro-spinal syphilis in a child may lead to hemiplegia with a resultant paralysis of arm or leg or both, marked mental defect, frequently associated with epileptiform seizures, and ultimately, in some cases, to juvenile general paralysis and tabes. Cooke and Jeans have shown that over 20 per cent. of all their cases of congenital syphilis had some involvement of the central nervous system, and my own observation of nearly 400 cases has also produced similar results (23 per cent. positive).

It should be noted that inherited neuro-syphilis may be latent and undetected except by examination of the cerebro-spinal fluid, consequently all cases of inherited syphilis should have a spinal fluid test at the commence-

TREATMENT OF INHERITED SYPHILIS

ment of the treatment, because if the fluid is positive, it is an indication that the treatment given should be more intensive, and of course, the fluid must be re-tested from time to time in order to ascertain when it becomes negative. In this way, which may be called the preventive method, one can ascertain at an early stage of the treatment if the fluid is positive, and by energetic measures sometimes prevent the occurrence of the later tragic manifestations mentioned above.

In connection with syphilis of the central nervous system there is a symptom of considerable importance which, however, is often overlooked, namely, inequality of the pupils with or without reaction to light and accommodation.

According to Kinnier Wilson * an ependymitis or subependymitis is not uncommon in syphilis, and the syphilitic toxin may possibly be able to filter through, so as to affect the periaqueductal fibres or terminal sensory aborisations, which are concerned with pupillary movements. Inequality of the pupils is not pathognomonic of syphilis, but its presence should make one very strongly suspicious of syphilis, and the disease should accordingly be carefully looked for. Only a week or two ago I saw a child, eight years of age, whom I had seen in infancy with symptoms of infantile congenital syphilis. The physician, under whose care he was, treated him with mercury only, and after a few months of this treatment the mother failed to bring the child up to hospital again, and in spite of all attempts to trace her she disappeared from our observation. Quite recently, in April of this year, I was able to re-establish contact with the family and had the child brought to me. He is now small for his age and somewhat troublesome at home with his brothers and sisters. Apart from very slight flattening of the nose there is not much in his appearance to suggest the presence of congenital syphilis, but the right pupil is distinctly bigger than the left and the teeth are suggestive. I performed a lumbar puncture on the child and his spinal fluid is very strongly positive. The mother tells me that the child had recently been examined by a school doctor and passed as normal in spite of the inequality of the pupil and suggestive Hutchinsonian teeth.

* S. A. KINNIER WILSON, *Journal of Neurology and Psychopathology*, Vol. II., March, 1921, p. 1.

BRITISH JOURNAL OF VENEREAL DISEASES

It seems to me that if we undertake to inspect school children and to look after their welfare, the inspectors should have had special training, and one of the special points to which their attention should be directed is the recognition of the stigmata of inherited syphilis.

Another lesion connected with the central nervous system whose relation to syphilis I have seen overlooked on several occasions is spastic paralysis. It may be a monoplegia, a diplegia or possibly a paraplegia. I saw two cases of this nature in a ward at the same time. Both of them had had very severe surgical operations performed for the relief of adductor spasm, various nerves and muscles having been divided, but the root trouble had not been ascertained until the cases were becoming quite mental, and then the blood and cerebro-spinal fluid investigations showed the presence of a strong syphilitic infection, both patients eventually lapsing into a condition of juvenile general paralysis. Another dictum which I am therefore constantly preaching is to have a Wassermann test done in all cases of paralysis in children.

The relation of inherited syphilis to mental under-development is a debatable point, and a subject to which considerable attention has been paid. My colleagues at Great Ormond Street now usually ask me to carry out a blood and spinal fluid test upon these cases, but it is only in a small proportion of them that a positive result is obtained. On the other hand, a few of these cases I have found to be the children of a congenitally syphilitic mother, and I think it is possible that symptoms of mental under-development or of epilepsy may be manifested by the children of a congenitally syphilitic parent without the child giving a positive Wassermann reaction.

Bilateral hydrarthrosis, especially if it affects the knee joints, is usually recognised as being of a syphilitic nature, but if only one knee joint be involved, and more especially if the swelling be associated with some pain and local heat, the condition may be diagnosed as tubercle or some subacute infection of the joint. I saw such a case recently which was operated upon before a blood test was carried out and which proved to be syphilitic in nature and has since done well on anti-syphilitic treatment.

Interstitial keratitis, which is perhaps the commonest

TREATMENT OF INHERITED SYPHILIS

symptom of late inherited syphilis, is so well known as not to need any description. It may occur, though very rarely, at birth, or may start in adult life. The usual age of onset is from eight to fifteen years, according to Jonathan Hutchinson, but I have seen it occur in a child of two and a half years. There is, I believe, still difference of opinion amongst ophthalmologists as to the value of anti-specific treatment by injections, but my own experience of more than 100 cases has taught me that patients with interstitial keratitis do very well with arsenical injections, for I have never seen hazy corneæ result when the injection treatment is started early and efficiently given. There is no doubt, however, that interstitial keratitis may occur in patients who have already received a considerable amount of treatment for an earlier syphilitic lesion and whose blood W.R. has thereby been rendered negative. From this we must conclude, I think, that it is not safe to say that a patient is cured of his congenital syphilis even though his W.R. may have been negative for some years—until the age of twenty, or possibly twenty-five or even thirty years is reached.

THE TEETH IN CONGENITAL SYPHILIS

The characteristic notched and pegged teeth to which attention was first directed by Jonathan Hutchinson, and which are now always known by the name "Hutchinsonian teeth," are probably the best known and most easily recognised stigma of inherited syphilis. Unfortunately, from the point of view of the diagnosis of the disease, they do not occur in all cases; in fact, probably not more than 25 or 30 per cent. of patients over seven exhibit these teeth in their characteristic form, but when the minor degrees of Hutchinsonian teeth are carefully looked for, at least another 25 per cent. of congenitally syphilitic patients will be found to possess them. Such teeth may show slight narrowing towards the cutting edge, but with straight sides, or the sides may be curved, giving rise to the barrel-shaped tooth, and the cutting edge may be slightly concave, without showing the characteristic notch. My colleague, Mr. Pitts, the dental surgeon at the Hospital for Sick Children, has on several occasions sent a child for blood examination on account of such slight degrees of Hutchinsonian teeth, with the

BRITISH JOURNAL OF VENEREAL DISEASES

result that a latent case of congenital syphilis has thus been discovered. I recently diagnosed congenital syphilis in the mother of one of my young patients by the slightly suggestive appearance of the central incisor teeth, and on investigation of her family the diagnosis was confirmed. It is my belief that if these minor degrees of Hutchinsonian teeth and of Moon's molars (the dome-shaped or mulberry six-year-old molars) were more widely known and looked for, congenital syphilis would be more frequently discovered than is now the case.

The Hutchinsonian characteristics are seen only in the teeth of the second dentition, though some authorities hold that notching and pegging of the deciduous incisors may occur in inherited syphilis. Mr. Pitts does not share this view, though he is of opinion that marked hypoplasia of the milk teeth should arouse a suspicion of syphilis sufficient to warrant further investigation.

With regard to deafness, the third component of the Hutchinsonian triad, I have found this a rare symptom among my patients. There may be two reasons for this. (1) that the more thorough treatment they receive at the present time prevents the spirochæte or its toxin from acting on the auditory nerve, and (2) that most of my patients are under twelve years of age. We had an instructive case recently in which my assistant reported that a child, aged ten, was becoming progressively deaf although having treatment by injections of N.A.B. He suspected a syphilitic deafness, but on looking into the ears it was obvious that the meati were fully charged with wax, the removal of which was promptly followed by the restoration of the hearing.

When we come to consider the value of the Wassermann test in the diagnosis of inherited syphilis we all realise what an immense advantage the serological tests give us over the practitioners of former generations. The application of these tests has cleared up many of the obscurities which clouded and rendered so difficult of interpretation some of the clinical observations of pre-Wassermann days.

Two of the most important of these are: (1) the recognition of latent syphilis in the mothers of undoubted syphilitic children, and secondly, the recognition of a latent syphilis in children. I have elsewhere written about the interpretation of the W.R. in children (*Lancet*,

TREATMENT OF INHERITED SYPHILIS

January 12th, 1929), and to-night can only mention a few of the most important points in this connection.

In the first place we must remember that an infant at, or shortly after, birth, may show a positive Wassermann in its blood and yet not be syphilitic. Such a condition may be due to the passage of the Wassermann substance from the mother to the child, for on subsequent examination a few weeks later the child's blood may be found negative and the reaction may remain negative. In such a case and if the child shows no signs or symptoms of syphilis, it is generally held that the child is not syphilitic. On the other hand, by far the large majority of syphilitic infants give a strongly positive W.R. if signs or symptoms of syphilis are present, yet we must remember that occasionally a child with obvious congenital syphilis may give a negative W.R. for the first few months of life, and sometimes even much longer. I have already referred to an interesting case exemplifying this, in which a child, shortly after birth, gave a negative Wassermann, but at the age of three months, when epiphysitis was present, the W.R. was positive for a short time only, and since treatment has been quite negative. In older children, and in children born a number of years after the infection was introduced into the family, the W.R. may show weakly positive reactions. I am strongly of the opinion that when such a result is obtained it should not be disregarded, but should rather serve as a stimulus to enquire more minutely into the patient's own and the family history. In the presence of undoubted signs or symptoms of congenital syphilis either in infancy or later childhood, a negative W.R. should never be taken as conclusive evidence that the case is not syphilis. One mentions this because clinicians are frequently content to rely upon one negative W.R. and to think that the case therefore is not syphilitic.

In congenital neuro-syphilis the C.S. fluid usually shows evidence of the condition in the increase of protein (which, however, in my experience may be only slight), in the increase of the cell content, a positive W.R. and Lange curve. The most important of these findings is undoubtedly the positive W.R., and in treatment one's aim is always to make this negative, if possible, and if this end is attained one usually finds that the fluid remains negative. On the other hand, I have at least one case

BRITISH JOURNAL OF VENEREAL DISEASES

in my series in which there was an alternating W.R. shown by the fluid.

The points in connection with the Wassermann test which I wish to emphasise are :—

(1) The importance of having this test done in any doubtful case and certainly more often than is the custom at present.

(2) To treat as syphilitic any child with obvious manifestations in spite of a negative W.R., though it must be remembered that a negative W.R. in a child and its mother, if repeated after a provocative injection is strong evidence against syphilis.

(3) To treat as syphilitic apparently healthy children whose only symptom is a positive W.R.

(4) To examine the C.S. fluid in every case of inherited syphilis and if positive, to endeavour to make and keep it negative.

MERCURY IN TREATMENT

The fact that mercury has been used for probably at least 200 years in the treatment of inherited syphilis and that its value in treatment is credited—though less strongly than formerly—at the present day, is evidence of the efficacy of the drug. There is no doubt that vigorous inunction with ung. hydr. and the administration of grey powder or other preparation of mercury will sometimes clear the cutaneous and nasal lesions of inherited syphilis as if by magic. It is no wonder, therefore, that the older syphilologists regarded mercury as *the* specific for this disease and with the disappearance of the obvious manifestations looked upon the patient as cured. The statement will be frequently found in the writings of the older authors that the patient was given mercury and was cured in three months, six months and so forth. Only a few years ago when discussing the treatment of inherited syphilis with a colleague, he definitely told me that he had treated very many cases with mercury and had cured them. I wonder how many of these patients he saw again five, ten or twenty years afterwards, and what proportion of them developed late manifestations of the disease. The very fact that we recognise symptoms of late congenital syphilis is evidence to my mind that the treatment adopted has not cured the patient, though of course a small proportion of the cases probably had the

TREATMENT OF INHERITED SYPHILIS

disease so mildly in infancy that it was not recognised, and consequently not treated at all. I am quite prepared to admit that mercury adequately administered and over a sufficiently long period of time—at least two years—may cure a certain proportion of the cases of inherited syphilis treated in this way, but it is extremely difficult in hospital practice, and to a less extent in private practice, to be certain that the mother or nurse applies the treatment sufficiently thoroughly, and secondly, that the full two years' course is given.

It is not at all an uncommon experience in hospital practice to find that the mother brings the child, perhaps for two or three months, to obtain a renewal of the ointment and grey powder, and then, in spite of the advice of the physician or surgeon that she should come regularly for two years, she ceases to come because the child is seemingly well. Nobody apparently keeps a record of the non-attendance, and through the mother's negligence the child possibly may become a sufferer for the rest of its life. I have, in my series of cases, quite a considerable number where the sequence of events has been as I have indicated. For example, a marasmic child was brought to hospital on account of epiphysitis in October, 1914. His condition was diagnosed as congenital syphilis and he had inunctions of mercury for one month only. He was not brought back to hospital until eight years later, when he was thin and pale, and improved considerably after a few injections of Neo-kharsivan. His cerebrospinal fluid was examined and found to be positive. The boy now has optic atrophy and signs of early tabes.

Another child attended hospital for one year, having had the symptoms of early inherited syphilis, yet in spite of the fact that he attended two hospitals subsequently for various ailments, it was not until he was nine years old that a blood test was taken and then found to be very strongly positive. This child has had a large amount of treatment during the past three years, but his W.R. is still very strongly positive, and it is I think unlikely that he will ever be cured of the disease.

Another child to which I have already referred attended hospital for three months on account of snuffles and rash, after which treatment was discontinued through the mother's neglect to bring the child to hospital. Eight years afterwards I succeeded in tracing him again, and



BRITISH JOURNAL OF VENEREAL DISEASES

now I find his blood and C.S.F. both give a very strong positive W.R. These cases could be multiplied indefinitely, and in my view should not be permitted to occur. Even if a particular physician believes in the efficacy of mercury treatment and wishes to give this alone, there should be an efficient social service to see that the child is brought regularly to hospital. One must also bear in mind the possibility that the mother may not give the child the treatment which the physician prescribes, and that, in consequence, treatment by injections, when one knows that the patient is receiving the drug intended, is an advantage over oral treatment.

As showing the inefficacy of mercury even when given over a period of years I have several cases, some of which have attended Great Ormond Street and others at other children's hospitals regularly for eight or nine years, and yet who, when they came under observation at the end of that time had positive Wassermanns and evidence of active syphilis in them.

On the whole, therefore, I should be inclined to say that mercury is not a reliable drug to use by itself in the treatment of inherited syphilis, but that it should be given in association with some form of arsenic preparation.

OTHER FORMS OF TREATMENT

My own view is that once we have diagnosed the case as inherited syphilis, we ought to make up our minds to treat it with injections either of some arsenical or bismuth preparation. I think perhaps a word of warning should be given here when the treatment of young infants who are born with signs of the disease on them or who are severely infected, is concerned. On several occasions one has found that treatment by injection has had a fatal effect after the first, or more commonly, the second injection. It would seem that the spirochæticidal action of the drug liberates a flood of toxin in the child's body against which the frail organism is unable to defend itself. It is advisable in these cases to start with mercury for a few weeks and then to give injections of very small doses of arsenicals. Nowadays, since we have sulphostab and similar drugs which can be injected intramuscularly, it is unnecessary to give intravenous injections to very small children, and I, personally, have never given an

TREATMENT OF INHERITED SYPHILIS

infant an injection into the longitudinal sinus, and would never advise it to be done.

With regard to the duration of the treatment, it is rather difficult to be dogmatic, because even if the W.R. may remain negative for years, one can never be certain until the lapse of very many years and perhaps not until the end of life, that the patient has really been freed from all trace of the disease.

As a rule one finds when treating infants that the symptoms clear up rapidly under treatment, and the W.R. becomes negative, and it has been my practice in the past to give one further course of eight injections after the Wassermann has become quite negative. I am of the opinion, however, that I may have erred on the side of insufficient treatment, though I have done it with the object of inflicting the minimum of pain upon the child by the treatment, because in a certain number of the cases the W.R. has become positive again, perhaps in the course of the next twelve months, although no active manifestations of the disease were apparent. On this account I now prefer to give at least two courses after the W.R. has become negative or to continue the treatment for at least a year.

In older children the W.R. is much more difficult to influence, although the symptoms of the disease are lessened by the injections. On many occasions I have had to give as many as forty or more injections, and even after this the Wassermann has not become negative. Sometimes one finds that this Wassermann fastness is associated with a positive C.S.F., and in these cases I now give the patient malarial treatment or T.A.B. vaccine. I have noticed that in a few cases the Wassermann, which at the last test was strongly positive, when re-examined perhaps six or more years afterwards has become negative without any treatment having been given in the meantime.

I had rather an instructive case last year when a child was brought to me on account of eye trouble, and the mother informed me that she had been in one of the special eye institutions for over two years and had had treatment there. On enquiry I was informed by the Medical Officer that she had had 'a course of injections.' On further enquiry as to details of the treatment, I learnt that during the two years that she had been an

BRITISH JOURNAL OF VENEREAL DISEASES

inmate of the institution she had received four injections of sulfarsenol (0.6 grm.)! Now that we are giving her regular treatment her local symptoms and general condition are very much improved. One has come across similar instances where the treatment given has been totally inadequate.

In conclusion, Ladies and Gentlemen, I should like to assure you, if such assurance is required, that it is in no vainglorious or boastful spirit that I have read this paper to you, which might suggest that I am in any way better than my professional brethren. It happens that I have had exceptional opportunities and facilities for examining and treating a large number of cases of inherited syphilis, for which facilities I am much indebted to all my colleagues at the Hospital for Sick Children, Great Ormond Street. The difficulties in diagnosis and treatment which I have indicated to you may occur in the practice of any one of us, and my aim has been to point out some of these difficulties so that you may perhaps be the better enabled to lighten, or possibly entirely remove, the burden of suffering which a pitiless Fate has placed upon a number of innocent children and their mothers. Even with our modern methods of treatment we can never be absolutely sure that we have cured a case of inherited syphilis, therefore let us prevent the disease; and in my view no expectant syphilitic mother should be allowed to go through her period of pregnancy without appropriate treatment for the protection of her child.